DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
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Silver Spring, MD 20993-0002

April 21, 2015

IMMUNODIAGNOSTIC SYSTEMS LTD.
MICK FENTON, REGULATORY AFFAIRS OFFICER
10 DIDCOT WAY, BOLDEN BUSINESS PARK
BOLDON, TYNE & WEAR NE35 9PD
UNITED KINGDOM

Re: K142994
Trade/Device Name: IDS-iSYS Aldosterone,
IDS-iSYS Aldosterone Control Set,
IDS-iSYS Aldosterone Calibration Verifiers
Regulation Number: 21 CFR 862.1045
Regulation Name: Aldosterone test system
Regulatory Class: II
Product Code: CJM, JJX
Dated: February 6, 2015
Received: February 12, 2015

Dear Mr. Mick Fenton:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the

electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Katherine Serrano -S

For: Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
k142994

Device Name
IDS-iSYS Aldosterone
IDS-iSYS Aldosterone Control Set
IDS-iSYS Aldosterone Calibration Verifiers

Indications for Use *(Describe)*

The IDS-iSYS Aldosterone assay (IS-3300) is a device intended for use in clinical laboratories for the quantitative determination of Aldosterone in human EDTA plasma on the IDS-iSYS Multi-Discipline Automated System. Aldosterone measurements are used in the diagnosis and treatment of primary aldosteronism (a disorder caused by excessive secretion of Aldosterone by the adrenal gland), hypertension caused by primary aldosteronism, selective hyperaldosteronism, edematous states and other conditions of electrolyte balance.

The IDS-iSYS Aldosterone Control Set (IS-3330) is intended for use as assayed quality control samples to monitor the accuracy of the IDS-iSYS Aldosterone assay on the IDS-iSYS Multi-Discipline Automated System.

The IDS-iSYS Aldosterone Calibration Verifiers (IS-3335) are intended for medical purposes for use in the quantitative verification of calibration of the IDS-iSYS Aldosterone assay on the IDS-iSYS Multi-Discipline Automated System.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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k142994

510(k) SUMMARY

Introduction

According to the requirements of 21CFR807.92, the following information provides sufficient detail to understand the basis for a determination of substantial equivalence.

Submitter

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Date prepared: 04 April 2015

Device Name

Proprietary names:	IDS-iSYS Aldosterone IDS-iSYS Aldosterone Control Set IDS-iSYS Aldosterone Calibration Verifiers
Common names:	As above
Classification:	21CFR862.1045 (Class II) 21CFR862.1660 (Class I, Reserved)
Product Code:	CJM JJX

Predicate Device

The IDS-iSYS Aldosterone assay is substantially equivalent to other products in commercial distribution intended for similar use. We claim equivalency to the currently marketed Siemens Healthcare Diagnostics Ltd. Coat-A-Count® Aldosterone; TKAL 6615154 (K831178).

The IDS-iSYS Aldosterone Calibration Verifiers are substantially equivalent to other products in commercial distribution intended for similar use. We claim equivalency to the currently marketed

IDS-iSYS 25-Hydroxy Vitamin DS Calibration Verifiers (K111650).
The IDS-iSYS Aldosterone Control Set is substantially equivalent to other products in commercial distribution intended for similar use. We claim equivalency to the currently marketed IDS-iSYS 25-Hydroxy Vitamin DS Control Set (K091849).

Device Description

The IDS-iSYS Aldosterone assay is based on chemiluminescence technology. A biotinylated monoclonal anti-Aldosterone antibody is incubated with the sample, after an incubation step an Aldosterone acridinium conjugate is added and after a further incubation step streptavidin coated magnetic particles are added. Following a third incubation step the particles are "captured" using a magnet. After a washing step and addition of trigger reagents, the light emitted by the acridinium label is inversely proportional to the concentration of Aldosterone in the original sample.

Intended Use

The IDS-iSYS Aldosterone assay (IS-3300) is a device intended for use in clinical laboratories for the quantitative determination of Aldosterone in human EDTA plasma on the IDS-iSYS Multi-Discipline Automated System. Aldosterone measurements are used in the diagnosis and treatment of primary aldosteronism (a disorder caused by excessive secretion of Aldosterone by the adrenal gland), hypertension caused by primary aldosteronism, selective hyperaldosteronism, edematous states and other conditions of electrolyte balance.

The IDS-iSYS Aldosterone Control Set (IS-3330) is intended for use as assayed quality control samples to monitor the accuracy of the IDS-iSYS Aldosterone assay on the IDS-iSYS Multi-Discipline Automated System.

The IDS-iSYS Aldosterone Calibration Verifiers (IS-3335) is a device intended for medical purposes for use in the quantitative verification of calibration of the IDS-iSYS Aldosterone assay when performed on the IDS-iSYS Multi-Discipline Automated System.

Comparison Table Table 1 Similarities and differences

Performance	**Predicate**	**New device**
Intended Use	IVD; For the quantitative measurement of aldosterone in serum (or heparin/EDTA plasma)	IVD; For the quantitative measurement of aldosterone in EDTA plasma
Analyte	Aldosterone	same
Sample matrix (primary tube type)	EDTA plasma	same

Calibrators -matrix	Lyophilised human serum	same
Reagent storage	2-8°C	same
Sample volume	200µl	same
Range of assay	2.5 to120 ng/dL (reported as 25 – 1200 pg/mL)	3.9 to 120 ng/dL
Spiking recovery	Average 96.1% [range 86-111% between 232-847 pg/mL (23.2 - 84.7 ng/dL)]	Average 94.8% [range 77-107.9% between 27.2-71.3ng/dL]
Analytical specificity	**Bilirubin:** Presence of bilirubin in concentrations of up to 200 mg/L has no effect on results, within the precision of the assay. **Hemolysis:** Presence of packed red blood cells in concentrations up to 30 µL/mL has no effect on results, within the precision of the assay. **Lipemia:** the 600 pg/mL calibrator was serially diluted with each of two lipemic serum pools, results showed excellent recoveries, even in presence of severe lipemia.	**Potentially Interfering Agent** / **Threshold Concentration** Triglyceride 500 mg/dL Haemoglobin 200 mg/dL Bilirubin 15 mg/dL Albumin 8 g/dL Red Blood Cells 0.2% Biotin 22 nM Rheumatoid Factor 1000 IU/mL Human anti-mouse Antibodies (HAMA) 30 ng/mL
Antibody	Antiserum against aldosterone (species origin not stated)	Monoclonal mouse-anti-aldosterone antibody
Capture	Antibody-coated polypropylene tubes	Streptavidin covalently coupled to paramagnetic particles
Method of detection	Radioactivity using ^{125}I-labelled aldosterone	Chemiluminescence using an acridinium-ester derivative
Analytical sensitivity	11 pg/mL (1.1 ng/dL)	3.2 ng/dL
Linearity	The assay has a tendency to over-recover upon dilution. Patient samples having values greater than the highest calibrator (1200pg/mL) can be reported as greater than 1200 pg/mL or diluted using a serum pool. Dilution with the zero calibrator is not recommended. The uncorrected value observed after dilution should be greater than 600 pg/mL.	y=1.00x – 1.24ng/dL; r^2 = 1.00
Precision	Intra-assay: 5.4 - 2.3% at 65-813 pg/mL (6.5 - 81.3 ng/dL) Inter-assay: 15.7- 3.8% at 58-548 pg/mL (5.8 – 54.8 ng/dL)	Within-Run: 8.4-2.2% at 7.5 – 98.7 ng/dL Total: 12.8-5.2% at 7.5 – 98.7 ng/dL
Reference range	Standing: 4 – 31 ng/dL Recumbent: 1 – 16 ng/dL	Female Supine: 3.9- 33.6 ng/dL Female Upright:3.9 – 50.1 ng/dL Male Supine: 3.9 – 19.5 ng/dL Male Upright: 3.9 – 23.2 ng/dL

Cross-reactivity	**Analyte**	**Cross-Reactivity**	**Analyte**	**Cross-Reactivity**
	Aldosterone	100%	Aldosterone	100%
	Androstenedione	Not detectable	Androstenedione	<0.001%
	Androsterone	0.0005%	Androsterone	0.0003%
	Corticosterone	0.002%	Cortisol	<0.001%
	18-OH-corticosterone	0.033%	11-Deoxycortisol	<0.001%
	Cortisol	Not detectable	Cortisone	<0.001%
	Cortisone	0.0003%	Corticosterone	<0.001%
	11-Deoxycorticosterone	0.006%	11-Deoxy-corticosterone	<0.001%
	11-Deoxycortisol	0.0004%	18-OH-corticosterone	0.2%
	Dexamethasone	0.00005%	Dexamethasone	<0.001%
	DHEA	0.0005%	DHEA	<0.001%
	Estradiol	Not detectable	Estradiol	<0.001%
	Estriol	Not detectable	Estrone	<0.001%
	Estrone	Not detectable	Prednisone	<0.001%
	Fludrocortisone	Not detectable	Prednisolone	<0.001%
	Prazosin	0.00003%	Progesterone	<0.001%
	Prednisolone	Not detectable	Spironolactone	<0.001%
	Prednisone	Not detectable	Testosterone	<0.001%
	Pregnenolone	Not detectable	Prazosin HCl	<0.001%
	Progesterone	0.007%	Verapamil HCl	<0.001%
	17α-OH-Progesterone	Not detectable	Doxazosin mesylate	<0.001%
	Spironolactone	0.06%	Fludrocortisone acetate	<0.001%
	Testosterone	Not detectable	Cholesterol	<0.001%
			3α, 5β-Tetrahydoaldosterone	3.1%
Automation	Manual assay		Automated assay	
Onboard reagent stability	N/A		35 days	
Calibration	Full standard curve to be run with each assay run		Uses a Master Curve and a two-point, user-initiated calibration to calibrate the assay. The system stores the calibration for the interval specified in the kit IFU.	

Calibrators – number of vials	7 levels including the zero	2 levels
Calibration interval	Per assay run	4 days
Assay duration	Minimum 18hours (overnight incubation)	43 minutes to first result
Quality Control	A tri-level, human serum-based immunoassay control, containing aldosterone as one of over 25 constituents, is available from Siemens Healthcare Diagnostics, not included in the kit (catalogue number: CON6)	Requires three serum-based quality control samples to verify the calibration. The control samples are supplied in a separate Kit.
Kit components of Reagent Kit	- Aldosterone Antibody-coated tubes (TAL1) - ^{125}I-Aldosterone tracer (TAL2) - Aldosterone Calibrators A through G (ALC3-9)	- Reagent cartridge of: Streptavidin-Magnetic particles, Aldosterone-Acridinium conjugate tracer, Biotinylated anti-aldosterone antibody, Assay buffer - Two levels of Calibrators (A&B) - Mini CD
Kit components of Controls Set	N/A	- Three levels of assay controls (6 vials per level, 1mL per vial) - Mini CD
Method Comparison	N/A	IDS-iSYS = 1.070 (x) – 0.29, R2=0.98, n=161 x= Diasorin Liaison Aldosterone
IDS-iSYS Aldosterone Calibration Verifiers	IDS-iSYS 25OHD^{s} Calibration Verifiers	New Device
Similarities		
Intended use/ Indications for use	Intended for medical purposes for use in the quantitative verification of calibration and assay measurable range of the IDS-iSYS	The same
Levels	Four	Four
Unopened Stability	Six months	Six months
Differences		
Format	Ready to use	Lyophilized
Analyte	25-Hydroxy Vitamin D	Aldosterone
Matrix	Horse serum	Human serum
Reconstituted Stability	2.5 hours	4 hours

IDS-iSYS Aldosterone Control Set	IDS-iSYS 25OHD Control Set	New Device
Similarities		
Intended use/ Indications for use	Intended for medical purposes for used for quality control of the assay	The same

	on the IDS-iSYS Multi-Discipline Automated System.	
Levels	Three	Three
Unopened Stability	Six months	Six months
Differences		
Format	Ready to use	Lyophilized
Analyte	25-Hydroxy Vitamin D	Aldosterone
Matrix	Horse serum	Human serum
Reconstituted Stability	2.5 hours	4 hours

Performance Characteristics

1. Analytical performance:

a. Precision/Reproducibility:
Precision was determined in accordance with CLSI EP5-A2, "Evaluation of Precision Performance of Quantitative Measurement Methods". Assessment was made for the following variables:

- within run precision;

- between run precision

- total precision

Precision studies were performed on two sites using three analyzers and three manufacturing batches (cartridge reagents and calibrators) by four operators.

To assess the variables of reproducibility, three lots of IDS-iSYS Aldosterone assay reagents were used to assay nine samples over a minimum of 20 assay days. Samples were assayed in duplicate, twice a day, to provide 80 replicates over 40 runs. Three instruments were used with each reagent batch and operated by a total of four personnel during the study. The sample concentrations were interpolated by using two-point calibration (Kit Cal A and B) as intended for use by the end user.

The data used to provide the claims to be inserted in the Labelling were obtained from six EDTA plasma samples which were assayed using three lots of reagents. The samples were run in duplicate twice per day for 20 days on 2 instruments and are the following:

Concentration ng/dL (pmol/L)	n	Within-run		Total	
		SD	CV%	SD	CV%
7.5 (208)	80	0.6	8.4	1.0	12.8
21.5 (594)	80	1.0	4.8	1.5	6.9
29.3 (812)	80	0.9	3.2	1.6	5.5
49.3 (1366)	80	1.6	3.3	2.6	5.2
65.7 (1820)	80	1.4	2.2	4.1	6.2
98.7 (2734)	80	4.0	4.1	5.9	6.0

b. Linearity/Assay Reportable Range:

The linear range of the assay was determined following a protocol based on the CLSI guidance EP6-A "Evaluation of the linearity of quantitative measurement procedures: a statistical approach".

A high plasma sample with aldosterone concentrations at 133.6ng/dL was diluted with a low sample at 2.7 ng/dL in order to assess the linearity covering the range below and including the LoQ. The 11 dilution samples were run in quadruplicate with one reagent batch. This one linearity data set was chosen in order to justify the claims to be included in the Instructions for use as it covered the entire claimed measuring range (LoQ 3.9 to 120 ng/dL).

The linear regression equation obtained when the observed results were plotted against the expected results was: $y = 1.00x - 1.24$, $R^2 = 1.00$

c. Traceability, Stability, Expected Values (controls, calibrators, or methods):

Traceability

The IDS-iSYS Aldosterone calibrators, controls and calibration verifiers are traceable to in-house reference calibrators produced by dissolving Aldosterone (≥95% HPLC; A9477Sigma-Aldrich) in Dioxane (anhydrous, 99.8%; 296309 Sigma-Aldrich). The concentration was calculated by UV quantitation using the molar extinction coefficient of ε =15000 at an absorbance of 240nm. Preparation was gravimetric with no adjustment.

Value Assignment:

Value assignment of the IDS-iSYS Aldosterone Kit Calibrators: for each manufacturing batch the new kit calibrator sets are run as 'unknowns' in duplicate in at least 20 assays on one analyser. The concentrations of the calibrators to be calculated by using Prism software package following issued QC procedures.

The concentration values obtained for the calibrators must fall within specified ranges. The data of 20 runs Internal Reference Calibrators are used to generate the logistic parameters of the Master calibration curve by using Prism software package. The calibrator concentration and master curve parameters are reagent batch specific and linked together. Verification of the calibration is performed by running three assays with On Board 2 point calibration on three different analyzers with controls of known levels.

The Kit Calibrator A and Calibrator B, when assayed by the user, provides an adjustment to trace the user's calibration curve to the master calibration curve for the specific reagents batch of IDS-iSYS Aldosterone kit.

Value assignment of the IDS-iSYS Aldosterone Kit Controls:
To assign acceptable ranges to the Kit Assay Controls (CTL1, CTL2 and CTL3), the controls are assayed in the IDS-iSYS Aldosterone assay with On Board 2 point calibration. The new Assay Controls are run in triplicate in at least 18 assays on a total of at least three analyzers. The acceptable range is then calculated as the mean ± 3 standard deviations for Kit Controls 1, 2, and 3, respectively.

Value assignment of the IDS-iSYS Aldosterone Calibration Verifiers:
The value allocation of calibration verifiers (CV0, 1, 2 and 3) is performed the same way as the Kit Assay controls.

Stability:

The stability of the IDS-iSYS Aldosterone assay Cartridge, Calibrators A and B, Kit Controls 1-3 and Calibration verifiers was derived from assessment by storage at various conditions, following EN 13640:2002 guideline (CLSI EP25-A), *Stability Testing of In Vitro Diagnostic Reagents*.

Reagent shelf life	**Cartridge**	**Calibrators**	**Controls**	**Calibration Verifiers**
Before opening at 2 - 8 °C	Six months		twelve months	Fifteen months
Cartridge, after opening at 2 - 8 °C	35 days	NA	NA	NA
On board the System	35 days	4 Hours	4 Hours	4 Hours
Frozen at ≤-20°C	N/A	5 weeks	5 weeks	5 weeks

d. Detection limit:

Study Protocol

The limit of blank (LoB) and limit of detection (LoD) and limit of quantitation (LoQ) were determined based on guidance from CLSI EP17-A "Protocols for the determination of limits of detection and limits of quantitation"

LoB, LoD and LoQ for two reagent lots were performed on 2 different analyzers, at two different sites. For the first reagent lot the LoB was determined in a plasma sample with zero aldosterone levels, in 10 replicates for 5 separate days for a total of 50 replicates. The resulting LoB level was 1.71 ng/dL. The LoD and LoQ for the same reagent batch were determined in 7 samples (concentrations ranging from 2.1 to 8.8ng/dL), run in 2 replicates, once per day

for 8 days. The resulting parametric LoD was 3.05 ng/dL and the LoQ at 20% CV was 3.9 ng/dL.

For the second reagent lot the LoB was determined in another plasma sample with zero aldosterone levels, in 6 replicates for 5 separate days for a total of 30 replicates. The resulting LoB was 2.03 ng/dL. The LoD in the second reagent lot was determined in 8 samples (with concentrations between 0.31 and 8.5 ng/dL), run in 2 replicates, once per day for 5 days. The LoD was determined in 7 samples (with concentrations between 1.1 and 7.8 ng/dL), run in 2 replicates, once per day for 5 days. The resulting LoQ was 3.8 ng/dL. In each case for the LoB, LoD and LoQ the highest values were taken for the Instruction for use claims.

LoB	2.0 ng/dL (55.4 pmol/L)
LoD	3.2 ng/dL (88.6 pmol/L)
LoQ	3.9 ng/dL (108 pmol/L)

e. Analytical specificity:

The sponsor performed interference and cross-reactivity studies were in accordance with CLSI guidance EP7-A2“Interference testing in clinical chemistry”.

Interference Screen testing was performed for the following substances: Triglycerides, Haemoglobin, Bilirubin, protein (albumin), Human anti-mouse antibody (HAMA), Red Blood Cells, Biotin and Rheumatoid Factor. To determine potential interference in the specific detection of Aldosterone, two base plasma samples, one in the range of approximately 10ng/dL Aldosterone (“Low”) and another at approximately 40ng/dL (“High”), were spiked with the potential interferent. Control samples (blank) were spiked with a volume of relevant diluent equal to that of the spiked interferent. The mean of 26 replicates, for both spiked and control samples (Blank), were then compared. One reagent batch was used for interference testing. The differences observed between the mean spiked and control sample values were examined and assessed according to acceptance criteria of ≤10% concentration bias to the unspiked sample.

All interferent spiking was performed just prior the assay.

In the case of protein interference, the native content was first measured by the Bradford test before the albumin spiking was performed.

% Interference was calculated using the formula % Interference = (mean spiked value - mean control value) / mean control value x 100

Interference was tested on two base plasma samples at two different clinically relevant Aldosterone concentrations. One Aldosterone level sample was used

with approx 10-15 ng/dL concentration. Where a neat sample at the desired concentration was not available Aldosterone was spiked into plasma pools created from various low Aldosterone content native plasma samples. Similarly for the high sample Aldosterone was either spiked into plasma pools (at approx. 40-60ng/dL) or native high sample pools were created to assess the interference at the higher part of the assay range. The interference materials were spiked into both samples. The baseline concentrations (Blank) were established in 26 replicates during the interference measurement. The control and interferent spiked samples (test) were measured in alternating order.

In the case of protein interference testing, the native protein content in the sample was first measured by the Bradford test to ascertain if the native content was at the level required in the specifications (6g/dL). If the native protein content was lower then human serum albumin (HSA) was spiked to bring the concentration up to 6g/dL and this was used to compare the interference in Aldosterone levels with the same sample spiked to 8g/dL HSA. The Bradford test was therefore carried out at least twice following the spiking of HSA and the sample was then put to the iSYS analyzer for determination of Aldosterone levels.

Stock solutions of each interferent were prepared in a diluent appropriate for the particular substance to be tested for interference (in most cases Scantibodies charcoal stripped lipid stripped serum). Samples were then spiked with the stock solution to a defined concentration of the potential interferent. Un-spiked control (Blank) samples were prepared using an equivalent volume of the diluent used to prepare the potential interfering substance.

Percent interference was calculated using the formula below:

$$\% \text{ Interference} = \frac{(\text{mean spiked concentration} - \text{mean un-spiked concentration})}{\text{mean un-spiked concentration}} \times 100$$

For assessing RF interference, recovery and linearity studies were performed. One plasma RF sample was used to compare the observed versus expected recovery by using ~10ng/dL and ~40ng/dL spiking with aldosterone antigen. The percent recoveries were calculated using the following calculation:

Recovery = Obs mean spiked value – Obs mean unspiked value

% Recovery = (Observed Recovery value / Expected Recovery value (Analyte added)) x 100

Cross-reactivity experiments were performed from stock materials prepared gravimetrically to a top dose (up to 200000x the Aldosterone assay top dose). Cross-reactivity was defined as the point where the reduction in signal corresponds to 50% of the signal achieved in the absence of analyte (B/Bo of 50%), as a percentage of the analyte concentration giving the same fall in signal

$$\% \text{ Cross-reactivity} = \frac{\text{ED50 (ng/dL) Aldosterone}}{\text{ED50 (ng/dL) compound}}$$

Stock concentrations of the substances to be checked for cross-reactivity were prepared initially in an organic solvent. This stock solution of the cross-reactant

was then spiked into Scantibodies serum with zero aldosterone concentration and subsequently diluted down serially to create a 7-point standard curve for each substance. Curves were run in the same experiment for comparison of ED-50 values of the potential cross-reactant against the ED50 of the Aldosterone assay displacement curve.

Result Summary

Potentially Interfering Agent	Threshold Concentration
Triglyceride	500mg/dL
Haemoglobin	200mg/dL
Bilirubin	15mg/dL
Albumin	8g/dL
Red Blood Cells	0.2%
Biotin	22nM
Rheumatoid Factor	1000IU/mL
Human anti-mouse Antibodies (HAMA)	30ng/mL

Limitations stated in the package inset:
In patients receiving therapy with a high biotin dose (i.e. >5 mg/day), no sample should be taken until at least 8 hours after the last biotin administration.

Hemolyzed samples should not be used with this assay.

Analyte	Cross-Reactivity
Aldosterone	100%
Androstenedione	<0.001%
Androsterone	<0.001%
Cortisol	<0.001%
11-Deoxycortisol	<0.001%
Cortisone	<0.001%
Corticosterone	<0.001%
11-Deoxycorticosterone	<0.001%
18-Hydroxycorticosterone	0.2%
Dexamethasone	<0.001%
DHEA	<0.001%
Estradiol	<0.001%
Estrone	<0.001%
Prednisone	<0.001%
Prednisolone	<0.001%
Pregnenolone	<0.001%
Progesterone	<0.001%
Spironolactone	<0.001%
Testosterone	<0.001%
Prazosin HCl	<0.001%
Verapamil HCl	<0.001%
Doxazosin mesylate	<0.001%
Fludrocortisone acetate	<0.001%
Cholesterol	<0.001%
3α, 5β-Tetrahydoaldosterone	3.1%

2. Comparison Studies:

Correlation studies based on guidance from the CLSI protocol EP9-A2 were performed to compare the IDS-iSYS Aldosterone assay and the Diasorin Liaison Aldosterone assay (previously cleared in k130321). The results of the statistical methods used for comparison of agreement between the IDS-iSYS Aldosterone

assay and the Liaison Aldosterone assay in 161 samples (including 12 altered samples) were as follows:

The linear regression correlation of the IDS-iSYS to the Diasorin Aldosterone assay in this set of plasma samples gave a slope of 1.053 (95%CI: 1.029 to 1.076) and intercept of 0.09ng/dL (95%CI: -0.86 to 1.05), R2= 0.980. Sample range tested was 3.9 – 110.9 ng/dL on the candidate device and 3.0 – 98.0 ng/dL on the comparative device.

Passing-Bablok analysis of the same data gave an intercept of -0.29 (95%CI: -0.98 to 0.46) and slope of 1.070 (95%CI: 1.043 to 1.096).

3. Reference range study (Expected values):

In order to determine the normal ranges for the IDS-iSYS Aldosterone assay, 228 Caucasian adult samples, collected in the US, 18-65 years of age, with normal blood pressure (systolic/diastolic ≤120/80) and normal BMI (18.5-24.9) were analysed using the IDS-iSYS Aldosterone assay. Samples were taken between 7-10am after overnight fasting, upright (30 minutes standing or walking) and supine (lying down for at least 30 minutes). The results obtained are given in the table below:

	n	Mean	SD	Range (Central 95%)
Female Supine	55	9.9 ng/dL (274 pmol/L)	9.4 ng/dL	<3.9 ng/dL-33.6 ng/dL
Female Upright	56	13.8 ng/dL (382 pmol/L)	11.9 ng/dL	<3.9 ng/dL-50.1 ng/dL
Male Supine	56	5.1 ng/dL (141 pmol/L)	4.7 ng/dL	<3.9 ng/dL-19.5 ng/dL
Male Upright	61	7.8 ng/dL (216 pmol/L)	4.8 ng/dL	<3.9 ng/dL-23.2 ng/dL

Conclusion

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.